

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 1-3, 6-19, 21, and 42-58 are pending. Claims 2, 3, 11, 12, and 42-58 are withdrawn as being drawn to a non-elected invention in response to a restriction requirement. Thus, claims 1, 6-10, 13-19, and 21 currently are under examination.

Examiner Interview

Applicants thank Examiners Noble and Crouch for the courtesy extended to their representative, Melissa E. Kolom, during the telephonic interview held on March 17, 2009. The matters discussed during the interview are substantially as set forth herein.

Discussion of Obviousness Rejection

Claims 1, 6-10, 13-19, and 21 remain rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Gu et al., *Vaccine*, 17: 340-344 (1999) (“the Gu reference”), Wu et al., *Proc. Natl. Acad. Sci. USA*, 92: 11671-11674 (1995) (“the Wu reference”), Farina et al., *J. Virol.*, 75: 11603-11613 (2001) (“the Farina reference”), Mogridge et al., *J. Bacteriol.*, 183: 2111-2116 (2001) (“the Mogridge reference”), and Hamdan et al., *Parasitol Res.*, 88: 583-586 (2002) (“the Hamdan reference”). This rejection is traversed for the reasons set forth below.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art “are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned Graham factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

Regarding the scope and content of the prior art, the Gu reference discloses a DNA plasmid vaccine encoding an immunogenic portion of *B. anthracis* protective antigen (PA). The Wu reference discloses a viral vector encoding the LAMP-1 signal peptide, the HPV16 E7 gene sequence, and the LAMP-1 sorting signal for use as a vaccine. Gene expression from the viral vector allegedly resulted in enhanced MHC II presentation of the E7 protein on antigen presenting cells (APC). The Wu reference also discloses that using a LAMP-1 sequence improves vaccine potency.

The Farina reference discloses a replication-defective vector based on a chimpanzee adenovirus which can be used as a vaccine construct. The Mogridge reference discloses a nucleic acid sequence encoding a mutated form of *B. anthracis* PA which exhibits impaired oligomerization ability. The Hamdan reference discloses a method of redesigning *S. manosoni* cDNA using recursive PCR and human-preferred codons. The Hamdan reference also suggests that codon optimization is a valuable method for improving heterologous expression of bacterial genes in human cells.

For the sake of argument and for purposes of the present analysis, one of ordinary skill in the art can be assumed to be someone with an advanced degree and a few years of experience in the relevant art.

According to the Office Action, it would have been obvious to one of ordinary skill in the art to modify the PA-encoding plasmid vaccine (as disclosed by the Gu reference) and employ a LAMP-1 sorting signal (as disclosed by the Wu reference) and a viral vector (as disclosed by the Wu and Farina references) using known recombinant DNA methodology to “predictably yield” the claimed gene transfer vector. The Office Action acknowledges that SEQ ID NO: 1 is not disclosed in the prior art. Nevertheless, the Office Action states that the Mogridge and Hamdan references disclose the process of codon optimization, specifically codon optimization of the PA gene, to improve the expression of an antigen in a mammalian cell. The Office Action contends that the invention defined by the pending claims is obvious because the cited references provide “a finite number of predictable codon optimized PA sequences, sorting signals, and viral vectors with a reasonable expectation of success” (Office

Action, pages 6-7, bridging paragraph). The clear implication in the Office Action is that there are a relatively small number of possible codon-optimized PA sequences.

Contrary to the allegations of the Office Action, the cited references do not describe a relatively small number of predictable codon-optimized PA sequences. In this regard, Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 of Ronald G. Crystal, which confirms that there are thousands of possible ways that the wild-type PA sequence could be modified via codon-optimization. Thus, it cannot be reasonably asserted that the cited prior art references, alone or in combination, disclose a relatively small number of predictable codon optimized PA sequences for one of ordinary skill in the art to systematically test, much less choose SEQ ID NO: 1. The Rule 132 Declaration also confirms that, contrary to the assertion of the Office Action, the Mogridge reference does not disclose codon-optimization of the PA gene. Rather, the Mogridge reference discloses mutations in domain 3 of the PA coding sequence generated via random mutagenesis, which mutations result in changes to the amino acid sequence of domain 3. In contrast, the modifications to the PA coding sequence disclosed in the present application occur across the entire PA coding sequence and do not alter the PA amino acid sequence encoded thereby.

For purposes of the analysis here, there is no need to consider any objective criteria of nonobviousness.

Based on the foregoing, Applicants submit that the cited references do not provide any disclosure or suggestion of the gene transfer vector of claim 1, particularly in view of the vast number of possible codon-optimized PA sequences. Moreover, as the Supreme Court recently stated, ‘*there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.*’ *KSR Int’l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)).” *Ex parte Wada and Murphy*, Appeal No. 2007-3733 (USPTO BPAI, January 14, 2008), slip op. at page 7. The cited references do not articulate a reason why one of ordinary skill in the art would be led to arrive at the particularly claimed PA sequence. Indeed, the cited references do not provide any indication or direction as to which of the numerous possibilities of codon-optimized PA sequences are successful.

As a result, one of ordinary skill in the art would not have found it "obvious to try" various codon-optimized PA sequences so as to arrive at a gene transfer vector comprising SEQ ID NO: 1. To assert otherwise, relies on improper and impermissible hindsight knowledge of Applicants' invention.

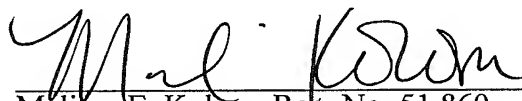
In considering whether or not the present invention is unobvious over the combination of the cited references, the Office must avoid the improper use of hindsight reconstruction, namely utilizing the pending claims as a template for selecting particular portions of particular references to combine in such a way so as to yield the present invention without any consideration of what one of ordinary skill in the art at the relevant time actually would have faced in seeking to solve the problem at hand. As stated by the Federal Circuit: "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.'" *Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 5 U.S.P.Q.2d 1788 (Fed. Cir. 1988).

Considering all of the Graham factors together, it is clear that the present invention would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combination of cited references. Accordingly, the obviousness rejections under Section 103 should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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